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REVIEW

*Clinical update*

# Coronary artery bypass grafting: Part 2—optimizing outcomes and future prospects

**Stuart J. Head[1], Jochen Börgermann[2], Ruben L.J. Osnabrugge[1], Teresa M. Kieser[3], Volkmar Falk[4], David P. Taggart[5], John D. Puskas[6], Jan F. Gummert[2], and Arie Pieter Kappetein[1]***

[1]Department of Cardiothoracic Surgery, Erasmus University Medical Centre, PO Box 2040, 3000 CA Rotterdam, The Netherlands; [2]Department of Cardiothoracic Surgery, Heart and Diabetes Centre North-Rhine Westphalia, Ruhr-University Bochum, Bad Oeynhausen, Germany; [3]Department of Cardiac Sciences, LIBIN Cardiovascular Institute of Alberta, University of Calgary, Calgary, Alberta, Canada; [4]Division of Cardiovascular Surgery, University Hospital Zurich, Zurich, Switzerland; [5]Department of Cardiovascular Surgery, John Radcliffe Hospital, Oxford University Hospitals NHS Trust, Oxford, UK; and [6]Division of Cardiothoracic Surgery, Emory University School of Medicine, Atlanta, GA, USA

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Since first introduced in the mid-1960s, coronary artery bypass grafting (CABG) has become the standard of care for patients with coronary artery disease. Surprisingly, the fundamental surgical technique itself did not change much over time. Nevertheless, outcomes after CABG have dramatically improved over the first 50 years. Randomized trials comparing percutaneous coronary intervention (PCI) to CABG have shown converging outcomes for select patient populations, providing more evidence for wider use of PCI. It is increasingly important to focus on the optimization of the short- and long-term outcomes of CABG and to reduce the level of invasiveness of this procedure. This review provides an overview on how new techniques and widespread consideration of evolving strategies have the potential to optimize outcomes after CABG. Such developments include off-pump CABG, clampless/anaortic CABG, minimally invasive CABG with or without extending to hybrid procedures, arterial revascularization, endoscopic vein harvesting, intraprocedural epiaortic scanning, graft flow assessment, and improved secondary prevention measures. In addition, this review represents a framework for future studies by summarizing the areas that need more rigorous clinical (randomized) evaluation.

**Keywords** Coronary artery bypass grafting • Off-pump • Anaortic • Minimally invasive • Hybrid revascularization • Arterial grafting • Endoscopic vein harvesting • Epiaortic scanning • Graft flow measurement • Secondary prevention • Guidelines • Heart team

## Introduction

Coronary artery bypass grafting (CABG) was first introduced in the mid-1960s and evolved rapidly as the standard of care for patients with extensive coronary artery disease.[1] However, the introduction of percutaneous coronary intervention (PCI) led to a reconsideration of therapeutic strategies.[2] Improvements in stent design, adjuvant medical therapy and technical skills quickly turned PCI into a very attractive alternative treatment option for patients with acute coronary syndromes and less complex coronary disease.[3–7] The broader use of PCI is reflected by declining CABG rates over the last decades,[8] even though recent long-term results from the SYNTAX,[9] ASCERT,[10] and FREEDOM[11] trials showed significantly better survival rates after CABG than after PCI. Despite converging outcomes between the two treatments in select patient populations, coronary surgery currently remains the standard of care for most elective patients, including those with diabetes and/or complex left main or three-vessel disease.[9,12]

Although short-term outcomes have dramatically improved over the first 50 years, surprisingly, technical aspects of the CABG procedure did not change significantly. Particularly in an era of increasing and sometimes overuse of PCI, several aspects of CABG should be improved to further optimize short- and long-term outcomes, while at the same time improving the appeal of CABG which is regarded as an overly invasive attractive treatment option by some. A number of advancements have been proposed, but adoption rates for these techniques are low.

This review provides a summary of how CABG outcomes can be optimized by adoption of new developments. These developments include off-pump, clampless/anaortic, and minimally invasive CABG

*Corresponding author. Tel: +31 (0)10 70 35784, Fax: +31 (0)10 70 33993, Email: a.kappetein@erasmusmc.nl

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with or without extending to hybrid procedures, arterial revascularization, endoscopic vein harvesting, intraprocedural epiaortic scanning and graft flow assessment and improved secondary prevention measures. Furthermore, this review represents a framework for future studies by summarizing the areas that need more rigorous clinical evaluation.

# Operative techniques

## Off-pump surgery

In 2001, ~25% of CABG procedures were performed off-pump.[13] In the Western world, the contemporary rate of off-pump CABG procedures is ~20%, while in Asia the majority of procedures is performed off-pump.[14] Theoretically off-pump CABG could reduce morbidity—particularly stroke—and even mortality by avoiding cardiopulmonary bypass that is associated with formation of microemboli, an increased blood–brain barrier permeability and aortic manipulation during cross-clamping and cannulation.[15]

Numerous risk-adjusted studies have found that the off-pump technique appears favourable in terms of both hard and surrogate endpoints.[16,17] A meta-analysis of propensity score-adjusted studies that included >120 000 patients demonstrated the superiority of the off-pump technique with respect to 11 selected short-term outcomes, particularly for mortality as the most important one (OR = 0.69; 95% CI: 0.60–0.75; $P < 0.0001$) and for stroke (OR = 0.42; 95% CI: 0.33–0.54; $P < 0.0001$).[18] In addition, the most recent meta-analysis of 59 randomized trials on a total of 8961 patients comparing on-pump with off-pump CABG demonstrated a 30% (95% CI: 1–51%) relative risk reduction for stroke.[13] However, some studies have shown increased rates of mortality and repeat revascularization during the follow-up;[19,20] probably caused by reduced graft patency after off-pump vs. on-pump CABG.[21,22] Although single-centre prospective angiographic studies have shown similar excellent graft patency rates with off-pump and on-pump CABG,[23] the 1-year results from the ROOBY trial showed a 27% higher risk of graft occlusion in the off-pump group (95% CI: 9–48%); graft patency was 87.8% in the on-pump and 82.6% in the off-pump patients ($P < 0.001$).[24] These results were criticized for the lack of sufficient experience that contributing surgeons had with off-pump procedures.[25] However, several other trials involving highly experienced surgeons and a meta-analysis pointed in a similar direction as the findings from the ROOBY trial.[25–27] Off-pump CABG has also been associated with increased rates of incomplete revascularization, and could result in reduced long-term survival.[28]

The CORONARY trial showed no benefit of off-pump CABG over on-pump CABG at 30 days or 1 year in 4752 randomized patients.[29,30] Although there appears to be a significant benefit of off-pump over on-pump CABG in patients at high-operative risk[31] and in patients with atherosclerotic aortas,[32] the hypothesis that off-pump CABG is beneficial for 'all-comers' may be too optimistic.[33] Despite the encouragement to a general use of off-pump techniques, it has been recommended specifically for high-risk patients.[34] However, even this recommendation was recently challenged by the results of the GOPCABE trial, which did include elderly higher-risk patients ($n = 2539$) but was still unable to confirm superiority of the off-pump over the on-pump approach in this subset of patients.[35] Patient selection is critical, since the majority of patients can safely and efficiently undergo on-pump CABG without the risk of increased 30-day repeat revascularization rates associated with off-pump procedures in the latest trials.[29,30,35] It may therefore be cumbersome for trainees to gain experience in a procedure with a steep learning curve that is infrequently performed only in selected patients.

It is worth noting that although evidence for a survival benefit of off-pump CABG is inconsistent across the peer-reviewed literature, a preponderance of evidence suggests that it is associated with significant reductions in transfusion requirements, prolonged ventilation, ICU and hospital length of stay, new renal failure, stroke/neurocognitive decline and other clinical endpoints.[36]

## Clampless/anaortic off-pump surgery

If off-pump CABG is performed, the degree of aortic manipulation should be reduced to a minimum. The benefit of off-pump CABG may be limited unless partial clamping of the aorta is avoided. Aortic clamping produces a significantly higher number of solid microemboli on transcranial Doppler than clampless surgery and can therefore lead to procedural stroke.[37] It is to note that in most trials, including the major randomized trials, off-pump CABG was not performed using an anaortic technique, the major driver for reducing stroke.

The number of studies that compared clampless CABG to 'regular' CABG with clamping is limited (*Table 1*). In the absence of a large randomized comparison, Börgermann *et al.*[38] used propensity matching to compare mortality and stroke rates between patients who underwent clampless off-pump or conventional CABG. In the propensity-matched cohort of 395 pairs, clampless off-pump CABG reduced rates of death (OR = 0.25, 95% CI: 0.05–1.18; $P = 0.080$) and stroke (OR = 0.36, 95% CI: 0.13–0.99; $P = 0.048$). More specifically, one of the largest studies to date found significantly lower stroke rates after off-pump than on-pump CABG, if an all-arterial 'no touch' technique was applied or when the proximal vein-graft anastomoses were performed clampless using the HeartString device (Guidant, Indianapolis, USA).[39] This evidence is complemented by a meta-analysis including 11 398 patients that showed that the absence of aortic manipulation was associated with a significant reduction of neurological complications (OR = 0.46, 95% CI: 0.29–0.72; $P = 0.0008$).[40]

## Minimally invasive coronary artery bypass grafting/hybrid revascularization

One of the drawbacks of CABG remains its invasiveness, even without the use of cardiopulmonary bypass. Quality of life scores at 30 days and patient treatment satisfaction surveys throughout the first 6 months are significantly higher after PCI than after CABG.[41] Moreover, CABG is sometimes referred to as a procedure where 'the chest is cracked open', which from a patient's perspective presents a frightening prospect of postoperative pain and extended rehabilitation. As a result, patients often prefer PCI to CABG because of 'temporal discounting', i.e. disproportionally emphasize short-term results even though CABG has been shown to be superior to PCI with respect to long-term survival and angina relief.[10,41–44]

**Table 1 Studies comparing clampless or 'aortic no touch' off-pump coronary artery bypass grafting with conventional off-pump or on-pump surgery**

| Author (year) | Inclusion | Design | No. of patients | Use of devices | Unadjusted 30-day outcomes | | | Comment |
|---|---|---|---|---|---|---|---|---|
| | | | | | Mortality | Stroke | Perioperative MI | |
| Clampless | | | | | | | | |
| Lev-Ran (2004) | 2000–02 | Retrospective | 103 vs. 57 with clamp | No | 2.9 vs. 7% | 0 vs. 5.3% | 3 vs. 5% | Side clamping an independent predictor of stroke or mortality: OR = 6.28, 95% CI: 1.39–28.4; $P = 0.017$ |
| Kempfert (2008) | 2003–05 | RCT | 51 vs. 48 with clamp | Connector: PAS-Port | 0 vs. 2.1% | — | — | |
| Manabe (2009) | 2004–07 | Retrospective | 109 vs. 185 no touch vs. 241 with clamp | HeartString ($n = 81$) Enclose II ($n = 28$) | 1.8 vs. 1.1 vs. 1.2% | 2.8 vs. 0.5 vs. 0.8% | — | |
| El Zayat (2012) | 2009 | RCT | 29 vs. 28 with clamp | HeartString | 0 vs. 0% | 0 vs. 6.9% | — | |
| Emmert (2012) | 1999–2009 | Prospective | 507 vs. 524 with clamp | HeartString | 1.8 vs. 2.5% | 0.4 vs. 2.9% | 1.5 vs. 3.1% | Clampless off-pump CABG was a significant predictor of reduced stroke in a propensity-score-adjusted analysis: OR = 0.04, 95% CI: 0.003–0.48 |
| Börgermann (2012) | 2009–10 | Prospective | 395 vs. 887 with clamp | Connector: PAS-Port ($n = 310$) | 3.3 vs. 7.6% | — | — | In a propensity-matched cohort of 395 pairs, clampless off-pump CABG was a predictor of less death (OR = 0.25, 95% CI: 0.05–1.18; $P = 0.080$) and stroke (OR = 0.36, 95% CI: 0.13–0.99; $P = 0.048$) |
| Aortic no touch | | | | | | | | |
| Patel (2002) | 1997–2001 | Prospective | 597 vs. 520 off-pump with manipulation vs. 1210 on-pump | No | 1.5 vs. 1.0 vs. 2.5% | 0.5 vs. 0.4 vs. 1.6% | — | Aortic manipulation was not a significant predictor of neurological outcome in off-pump patients |
| Calafiore (2002) | 1998–2000 | Retrospective | 1533 vs. 3290 any manipulation (on- or off-pump) | No | — | 0.2 vs. 1.4% | — | In multivariable stepwise logistic regression, any aortic manipulation was associated with an OR of 8.4 (95% CI: 2.4–28.9; $P = 0.0008$) for stroke |
| Kim (2002) | 1998–2001 | Prospective | 222 vs. 123 'regular' off-pump vs. 76 on-pump | No | 0.9 vs. 2.4 vs. 2.6% | 0 vs. 0.8 vs. 3.9% | 1.4 vs. 5.7 vs. 6.6% | |
| Leacche (2003) | 1996–2001 | Retrospective | 84 vs. 556 'regular' off-pump | No | 1.6 vs. 1.7% | 0 vs. 1% | 1.3 vs. 1.8% | |
| Kapetanakis (2004) | 1998–2002 | Retrospective | 476 vs. 2527 moderate vs. 4269 extensive aortic manipulation off-pump | No | 1.5 vs. 1.9 vs. 2.1% | 0.8 vs. 1.6 vs. 2.2% | 1.1 vs. 0.7 vs. 0.5% | No touch surgery was independently associated with reduced stroke when compared with extensive (OR = 1.7, 95% CI: 1.11–2.48; $P < 0.01$) and even moderate aortic manipulation (OR = 1.8, 95% CI: 1.15–2.74; $P < 0.01$). Propensity-matched analysis failed to show similar findings |
| Lev-Ran (2005) | 2000–03 | Retrospective | 471 vs. 229 off-pump with side-clamp | No | 2.1 vs. 2.6% | 0.2 vs. 2.2% | 1.4 vs. 1.5% | The use of side-clamping was an independent predictor of stroke: OR = 28.5, 95% CI: 2.27–333.3; $P = 0.009$ |
| Bolotin (2007) | 2000–01 | Prospective | 110 vs. 216 on-pump CABG | No | 2.7 vs. 1.9% | 0 vs. 2.3% | 0.9 vs. 1.4% | |

*Continued*

**Table 1** *Continued*

| Author (year) | Inclusion | Design | No. of patients | Use of devices | Unadjusted 30-day outcomes | | | Comment |
|---|---|---|---|---|---|---|---|---|
| | | | | | Mortality | Stroke | Perioperative MI | |
| Vallely (2008) | 2002–06 | Prospective | 1201 vs. 557 off-pump with aortic manipulation | No | 1.4 vs. 1.3% | 0.3 vs. 1.1% | 0.6 vs. 0.4% | No touch surgery was an independent predictor of reduced rates of neurological events: OR = 0.23, 95% CI: 0.06–0.92; $P = 0.037$ |
| Misfeld (2010) | 2002–07 | Retrospective | 1346 vs. 600 'regular' off-pump vs. 1753 on-pump | No | 1.0 vs. 1.0 vs. 2.3% | 0.1 vs. 0.5 vs. 0.9% | 0.5 vs. 0.5 vs. 0.6% | Compared to no touch off-pump CABG, on-pump CABG (OR = 12.3, 95% CI: 2.9–52.2; $P = 0.0006$) and 'regular' off-pump CABG (OR = 7.0, 95% CI: 1.4–35.0; $P = 0.018$) were independent predictors of neurological complications |
| Emmert (2011) | 2004–09 | Prospective | 1365 vs. 567 off-pump with clamp | HeartString | 1.8 vs. 1.6% | 0.7 vs 2.3% | 0.9 vs. 1.9% | No touch clampless off-pump CABG was a significant predictor of reduced stroke in a propensity score-adjusted analysis: OR = 0.39, 95% CI: 0.16–0.90; $P = 0.04$ |

CABG, coronary artery bypass grafting; MI, myocardial infarction; OR, odds ratio.

Less invasive surgical techniques may present an attractive alternative; minimally invasive direct coronary artery bypass (MIDCAB) does not require sternotomy and is therefore more acceptable to patients than conventional CABG.[45] The left minithoracotomy incision is smaller, the risk of scarring is less, and risks of deep sternal wound infection and problems with sternum healing are omitted. Although MIDCAB may be associated with slightly increased pain postoperatively due to spreading of the ribs, the length of stay is markedly reduced and there is an early postoperative quality of life benefit over conventional CABG.[46–48] MIDCAB was shown to be as safe and efficient as off-pump CABG, while reducing the recovery time.[49] Holzhey *et al.*[50] recently reported long-term results from their single-centre experience on 1768 patients. Five- and 10-year survival was 88.3 and 76.6%, respectively. The rates of freedom from major adverse cardiac or cerebrovascular events and angina were of 85.3 and 70.9%, respectively.

Exposure during MIDCAB is largely limited to the left anterior descending (LAD) artery and eventually diagonal branches, and therefore almost exclusively performed in patients with isolated LAD stenosis or occlusion. An open left internal mammary artery (IMA) graft to the LAD is without doubt the single most important conduit that offers a prognostic benefit based on its proven long-term patency and improved survival. Patients with multivessel disease—especially at younger age—also derive a survival benefit from total arterial grafting with bilateral IMA (BIMA) grafts.[51] The added benefit of a second arterial graft in older patients is less well documented;[52] however, the rate of early vein-graft failure, especially to distal targets and severely diseased small vessels, is high and ranges from 10 to 26% between 12 and 18 months after surgery.[21,53] In some patients, a hybrid procedure can combine the benefits of an MIDCAB—providing a left IMA (LIMA) graft to the LAD—and stenting of the circumflex and/or the right coronary artery. This type of management may yield results similar to those of a full CABG procedure,[54] but randomized trials are still lacking (*Table 2*). The hospitalization costs of hybrid revascularization are similar to the costs of off-pump CABG, but the time to return to work is shorter and patient satisfaction higher.[55] Halkos *et al.*[56,57] showed that survival after hybrid revascularization at 5-year follow-up was comparable with off-pump CABG in patients with left main disease (88.6 vs. 83.4%, respectively; $P = 0.55$) and in patients with multivessel disease (86.8 vs. 84.3%, respectively; $P = 0.61$) (*Figure 1*).

Complete revascularization in patients with multivessel disease by minimally invasive CABG can also be achieved via a totally endoscopic coronary artery bypass (TECAB) procedure,[58] by combining an endoscopic with an open approach,[59] or by a hybrid endoscopic and percutaneous procedure.[60] Such procedures are only performed in selected patients at specialized centres and require extensive operating times. Earlier series reported unsatisfactory patency results, but with the evolution of better endoscopic stabilizers the results from these highly experienced centres are similar to conventional CABG with a reported mortality rate of 1–2% [58–61] and a 5-year survival in the range of 85–95%.[60–62]

Adoption of minimally invasive CABG procedures has been slow. For MIDCAB, this may be explained in part by the low incidence of isolated proximal LAD stenosis[63] and also by the high technical demands of this procedure. Hybrid revascularization for multivessel disease, theoretically, has a much larger target population. However, a systematic search of the literature shows that the accumulated evidence is based on small non-randomized studies comprising just over 1000 patients in total (*Table 3*). Between October 2003 and April 2010, only 174 patients underwent hybrid revascularization in the USA.[56,57] Apart from technical issues, the low-adoption rate is partly due to logistic reasons; the staging of two procedures in a (hybrid) operating rooms, and/or catheterization laboratory, and the administration or discontinuation of antiplatelet therapy. A survey performed in 2002 indicated that 80% of US surgeons perform less than five MIDCAB procedures annually.[64] When asked about hybrid procedures, only 10% of surgeons were in favour. In contrast, 50% of 180 cardiologists were in favour of hybrid revascularization. Yet, only two cardiologists (1.1%) had referred patients for MIDCAB (with or without PCI). Stronger evidence to support a recommendation for hybrid revascularization is expected from a number of currently on-going registries, the largest of which is the Hybrid Revascularization Observational Study (NCT01121263) that includes patients throughout the USA and is sponsored by the National Heart, Lung, and Blood Institute (NHLBI).

**Table 2 Reasoning supporting hybrid revascularization**

| |
|---|
| Patients with double vessel disease and chronic total occlusion of the LAD |
| Patients with multivessel disease and an indication for CABG requiring complete revascularization in whom a full sternotomy is contraindicated or not desired |
| Patients with multivessel disease with a dominant LAD or complex proximal LAD lesion morphology and poor surgical targets in the distal CX or RCA territory amenable for PCI |
| Patients with multivessel disease with an indication for PCI (SYNTAX score <22) or in clinical trials comparing hybrid revascularization with PCI or CABG (SYNTAX score >23) |
| Patients with multivessel disease undergoing emergent PCI of a culprit lesion of a CX or RCA lesion (in the setting of STEMI, non-STEMI, or ACS) with a staged surgical revascularization of the LAD |

## Arterial grafting

The use of one IMA graft, most often the left IMA anastomosed to the LAD combined with venous conduits represents the standard therapy for patients undergoing CABG.[65,66] However, venous bypass grafts tend to fail: a recent study by Kim *et al.*[67] found that 11.8% of saphenous vein grafts failed within 7 days, which is similar to the failure rate reported by FitzGibbon *et al.*[68] Therefore, BIMA grafting should be strongly considered in patients with multivessel coronary disease, because BIMA grafting is associated with reduced mortality during the first year post-surgery and during the long-term follow-up.[69] A meta-analysis of seven pooled studies with 11 269 single and 4693 bilateral IMA grafts demonstrated that BIMA was associated with a reduced risk for death: HR = 0.81 (95% CI: 0.70–0.94).[51]

In the Arterial Revascularization Trial (ART), the only randomized trial to date comparing BIMA and single IMA (SIMA), 3102 patients were randomized in 28 centres in 7 countries.[70] Mortality rates at 30 days were 1.2% in both groups, and 2.3 vs. 2.5% at 1-year for SIMA and BIMA groups, respectively. There were also no differences in the incidence of stroke, MI, and repeat revascularization. While the use of a second IMA graft added 23 min to the operative procedure which in itself took 3–4 h, the trial clearly demonstrated that BIMA grafting was as safe as SIMA grafting, even though the risk of a need for later sternal reconstruction was increased: relative risk 3.24 (95% CI: 1.54–6.83). An extended follow-up (for up to 10 years) is expected for this study and will hopefully determine whether survival with BIMA grafts is indeed superior. The trial, however, also

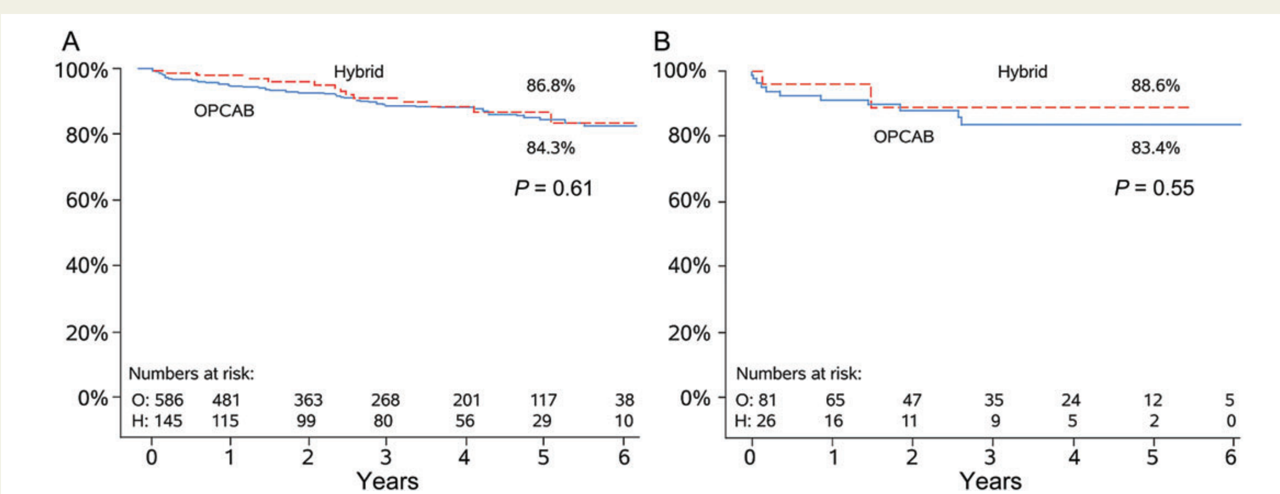


**Figure 1** Long-term survival of hybrid revascularization in comparison with off-pump coronary artery bypass grafting. A comparison between treatment strategies shows no differences in 5-year survival in patients with multivessel disease (*A*), nor in patients with left main disease (*B*). Adapted with permission from Halkos *et al.*[56,57]

**Table 3** Systematic review of studies evaluating hybrid revascularization

| Author (year) | Inclusion | Design | No. of patients | Type of lesions | Strategy | 30-day outcomes | | | Long-term outcomes | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Conversion | Death | Revascularization | Mean follow-up | Mortality | Revascularization |
| Lloyd (1999) | 1996–98 | Prospective | 18 | Multivessel | Simultaneous, $n = 4$<br>PCI following MIDCAB, $n = 14$ | 0 | 0 | 5.6% | At 18 months | 0 | 5.6% |
| Zenati (1999) | 1996–98 | Retrospective | 31 | Multivessel | Staged | 0 | 0 | 3.2% | 11 months | 0 | 9.6% |
| Wittwer (2000) | 1996–99 | — | 35 | Multivessel | PCI following MIDCAB | 0 | 0 | 0 | 11 ± 8 months | 0 | 6.5% (of 31 patients) |
| de Canniere (2001) | 1997–97 | Retrospective | 20 | Two-vessel | MIDCAB following PCI, $n = 9$<br>PCI following MIDCAB, $n = 11$ | 0 | 0 | 0 | At 2 years | 0 | 15% |
| Cisowski (2002) | 1999–2001 | Retrospective | 50 | Two-vessel | PCI following MIDCAB | 0 | 0 | 0 | — | 0 | 12.7% |
| Riess (2002) | 1997–2001 | Retrospective | 57 | Multivessel | PCI following MIDCAB | 0 | 0 | 0 | 101 ± 38 weeks | 1.8% | — |
| Stahl (2002) | — | Retrospective | 54 | Multivessel | PCI following MIDCAB, $n = 35$<br>MIDCAB following PCI, $n = 19$ | 0 | 0 | 0 | 12 months | 0 | — |
| Davidavicius (2005) | 2001–03 | Prospective | 20 | Multivessel | MIDCAB following PCI, $n = 14$<br>PCI following MIDCAB, $n = 6$ | 0 | 0 | 0 | 19 ± 10 months | 0 | 0 |
| Katz (2006) | — | Prospective | 27 | Two-vessel | Simultaneous, $n = 4$<br>PCI following MIDCAB, $n = 12$<br>MIDCAB following PCI, $n = 11$ | 0 | 0 | 0 | At 3 months | 0 | 18.5% |
| Us (2006) | 2002–04 | Prospective | 17 | Multivessel | MIDCAB following PCI | 0 | 0 | 0 | 21 ± 7 months | 0 | 17.6% |
| Gilard (2007) | 2000–. . . | Prospective | 70 | Multivessel | MIDCAB following PCI | 0 | 1.4% | 2.9% | 33 months | 1.4% | 0 |
| Holzhey (2008) | 1996–2007 | Retrospective | 117 | Multivessel | Simultaneous, $n = 5$<br>PCI following MIDCAB, $n = 59$<br>MIDCAB following PCI, $n = 53$ | 0 | 1.9% | 1.9% | 208 patient-years | 92.5% at 1 year<br>84.8% at 5 years | — |
| Kiaii (2008) | 2004–07 | Prospective | 58 | Two-vessel | Simultaneous | 1.7% | 0 | 0 | 20 months | 0 | — |
| Kon (2008) | 2005–06 | Prospective | 15 | Multivessel | Simultaneous | 0 | 0 | 0 | At 1 year | 0 | 6.7% |
| Gao (2009) | 2007–08 | Prospective | 10 | Multivessel | PCI following MIDCAB | 0 | 0 | 0 | 5 months | 0 | 0 |
| Vassiliades (2009) | 2003–07 | Prospective | 91 | Multivessel | Staged | 2.0% | 0 | 0 | — | 94% at 3 years | 5.5% at 1 year |
| Zhao (2009) | 2005–07 | Retrospective | 112 | Multivessel | Simultaneous | N/A | 2.6% | 0 | — | — | — |
| Delhaye (2010) | 2006–08 | Prospective | 18 | Multivessel | PCI following MIDCAB | 0 | 0 | 0 | At 1 year | 0 | 5.6% (TVR) |
| Halkos (2011) | 2003–10 | Retrospective | 27 | LM | PCI following MIDCAB | 0 | 0 | 0 | Median 3.2 years | 88.6% at 5 years | 7.4% |
| Halkos (2011) | 2003–10 | Retrospective | 147 | Multivessel | Simultaneous $n < 10$<br>Staged for the remaining | 0 | 0.7% | 0 | Median 3.2 years | 86.8% at 5 years | 12.2%<br>8.8% (TVR) |
| Hu (2011) | 2007–09 | Retrospective | 104 | Multivessel | Simultaneous | 1.0% | 0 | 0 | 18 months | 0 | 1.9% |
| Rab (2012) | 2003–. . . | Retrospective | 22 | LM | PCI following MIDCAB | 0 | 0 | 0 | 39 ± 23 | 4.5% | 0 |

The PubMed database was searched from its inception through June 2012, which yielded the included studies.
CABG, coronary artery bypass grafting; MIDCAB, minimally invasive coronary artery bypass; N/A, not applicable; LM, left main; PCI, percutaneous coronary intervention; TVR, target vessel revascularization.

highlighted the difficulties with BIMA grafting; 16.4% of patients randomized to BIMA did not receive the allocated treatment compared with 3.3% patients not receiving SIMA grafting.[71]

The proportion of procedures that are performed with IMA grafts is increasing, but a large inter-hospital variance remains. The use of at least one IMA can be as low as 45–65% in some centres, failing to provide optimal care to patients.[72] It is disconcerting that in the USA the use of BIMA grafts was only 4.0% among 541 368 patients.[72] The respective figures are 12% in Europe and 30% in Japan.[73] Among 1541 procedures performed in the SYNTAX trial and registry, 97.1% included a single arterial conduit while 22.7% received a second IMA graft. Owing to the technically more challenging and time-consuming nature of BIMA grafting, the fear of higher morbidity (i.e. sternal wound complications) and mortality, and the absence of clear randomized data showing a survival benefit, some surgeons may be reluctant to use BIMA grafts. Nevertheless, in order to improve CABG outcomes, the use of both IMA grafts should be considered more frequently.

When unilateral IMA grafting is performed, the saphenous vein is the most frequently chosen conduit for additional graft(s). Because of high failure rates of venous grafts, the radial artery has been investigated as an alternative. The long-term results from the RSVP trial ($n = 142$) suggested favourable radial artery graft patency rates.[74] More recent 5-year results from the larger randomized RAPS trial ($n = 510$) showed that, compared with the saphenous vein grafts, the radial artery had lower rates of functional graft occlusion (12.0 vs. 19.7%, respectively; $P = 0.03$) and complete occlusion (8.9 vs. 18.6%, respectively; $P = 0.002$), although the string sign was observed more frequently in radial artery grafts (3.4 vs. 0%, $P = 0.01$).[75] Several large observational studies have confirmed excellent graft patency and have even reported superior long-term survival rates,[76,77] also after applying propensity matching.[78–80] However, widespread utilization of the radial artery has been hampered by concerns regarding vessel spasm, graft atherosclerosis, and unfavourable results from a number of studies. The largest trial ($n = 733$) to date found no differences in graft patency at 1-year follow-up;[81] similar results have been reported from a number of observational studies.[79,82] At least one study has shown radial artery graft patency to be significantly worse than right IMA graft patency.[83] To ensure good graft patency, the radial artery should be used preferably in high-grade lesions.[84] Data from the STS database suggest that only 9% of CABG procedures are performed with the radial artery.[85]

A higher rate of disease progression to total occlusion in native coronaries has been reported after CABG than after PCI.[86] Patent arterial grafts, by virtue of their nitric oxide secreting properties, may protect against future atherosclerotic lesions. Therefore, arterial grafting can be viewed as a preventive measure that goes beyond pure treatment.[87,88]

## Endoscopic vein harvesting

Traditional open saphenous vein-graft harvesting requires a large incision, resulting in a large scar and a risk of postoperative wound complications. Endoscopic vein harvesting was introduced in the mid-1990s as an alternative.[89] This method has the advantages of reduced scarring, less pain, decreased postoperative complications, and shorter length of stay.[90]

Several randomized studies and meta-analyses have shown that endoscopic harvesting significantly reduces rates of wound infection, wound dehiscence, and overall complications.[91] However, subgroup analyses from the PREVENT IV and ROOBY randomized trials suggested that endoscopic vein harvesting resulted in reduced graft patency during the follow-up.[92,93] In PREVENT IV, there even were significantly higher rates of death. Although this is of potential concern, long-term follow-up analyses from large observational studies have not been able to confirm that clinical outcomes are worse in patients that underwent endoscopic vein harvesting.[94,95] A recent study that included 235 394 patients with 3-year follow-up showed no increased risk of mortality [adjusted HR = 1.00 (95% CI: 0.97–1.04) $P < 0.99$] or the composite of mortality, myocardial infarction, and repeat revascularization [adjusted HR = 1.00 (95% CI: 0.98–1.05) $P = 0.34$].[95]

Current data indicate a paradigm shift towards endoscopic harvesting as opposed to open vein graft harvesting. Between 2003 and 2008, 52% of grafts were harvested endoscopically at 989 sites in the USA; in 2008, the rate was already 70%.[95] Trainees in the USA now almost exclusively learn how to perform endoscopic harvesting.[90] It is important to start using this technique at an early stage, especially because inexperienced surgeons are known to cause significantly more vein injury.[96] The International Society of Minimally Invasive Cardiothoracic Surgery Consensus statement has given a Class IB recommendation for endoscopic vein harvesting.[97] Still, endoscopic harvesting is performed in only a minority of cases in Europe. A recent single-centre study showed that only 12.4% of veins were harvested endoscopically between 2008 and 2010.[98] Unfortunately, large-scale real-world data from European centres are scarce.

# Intra-operative assessments

## Epiaortic scanning

Atherosclerosis of the ascending aorta is present in >50% of patients undergoing CABG.[99] Aortic atherosclerosis was found to be a significant predictor of postoperative neurological events and renal failure, both caused by atheroembolism.[100,101] Palpation of the aorta is frequently employed prior to cannulation and/or aortic manipulation, but the sensitivity of this technique is very limited.[102] Therefore, imaging is advocated to detect atherosclerosis if an anaortic technique cannot be applied. Depending on the findings, the operative technique can be modified as needed.[103] Both transoesophageal echocardiography and epiaortic ultrasonography were introduced as methods for detecting severe atherosclerosis. While transoesophageal echocardiography severely underestimates the degree of atherosclerosis, epiaortic scanning is an easy, safe and efficient procedure and is preferred.[104]

Epiaortic scanning is not routinely used probably because of the cost of the machine (>€100 000) and the fact that there have been no direct randomized comparisons between CABG with and without epiaortic scanning that demonstrate a benefit. Such a study would be problematic because of the large sample size required. However, although one small study indicated no reduction in transcranial Doppler-detected cerebral emboli,[105] several studies have suggested that early postoperative stroke is significantly reduced when the operative technique is modified in accordance with results of epiaortic scanning.[106–109] Wareing *et al.*[110] reported that in 14% of elderly patients undergoing cardiac procedures (CABG in 89%), the site of aortic cannulation and/or clamping, the sites for attaching vein grafts, and/or the sites for instillation of cardioplegic solution were altered. The precise rates of such modifications provided in the literature vary, between 4 and 31%.[99] A recent study by Daniel *et al.*[111] showed that epiaortic scanning was increasingly performed from 2002 to 2009 (45 and 90%, respectively) and coincided with less frequent aortic clamping (98 and 73%, respectively).

### Graft flow measurement

Data from the PREVENT IV trial showed a suboptimal rate of saphenous vein-graft failure after on- and off-pump CABG at 1 year;[112] a meta-analysis reported a failure rate of ~5 and 25% at 3 and 12 months, respectively.[113] Several mechanisms of graft failure have been described. Early graft failure can occur as a result of anastomotic problems, limited outflow, graft kinking upon chest closure, and thrombosis. Late failure is the result of thrombosis and processes of intimal hyperplasia and atherosclerosis. Intra-operative graft assessment has been introduced to evaluate grafts and identify anastomotic problems and limited outflow. Disturbingly, Balacumaraswami *et al.*[114] demonstrated that intra-operative graft assessment identified 9% of grafts with inadequate flow in 25% of CABG patients, which led to revision in 3% of grafts and 8% of patients. Multiple techniques for intra-operative graft assessment have been proposed: coronary angiography, transit time flow measurement (TTFM), high-frequency epicardial echocardiography, thermal coronary angiography and intra-operative fluorescence imaging (IFI).[115] Although angiography is thought to be the best and most reliable method for assessing flow,[116] the infrastructure required for coronary angiography is rarely available in standard operating rooms. Wider implementation of hybrid operating rooms could potentially facilitate the use of coronary angiography. Currently, intra-operative graft assessment is most frequently performed by TTFM or IFI.

Both TTFM and IFI have strengths and weaknesses and have been criticized for their inability to identify grafts with minor abnormalities that present a risk for failure. Furthermore, inconsistent and variable measurements may lead to unnecessary graft revisions.[114] Two parameters, graft function and anatomy, are required for the complete assessment of bypass grafts. Transit time flow measurement assesses function and can very accurately detect truly poor and truly good grafts (true positives, true negatives), but there is an issue with respect to detecting poor grafts with a low pulsatility index (PI) (false negatives). False positives (good graft, high PI) rarely occur. Intra-operative fluorescence imaging evaluates anatomy but is associated with more inter-observer error than standard angiography. Comparisons between TTFM and IFI suggest that IFI is more sensitive.[113,114,117] Transit time flow measurement combined with epicardial ultrasonic scanning is a recently introduced approach that may provide both a functional as well as anatomic assessment.

Despite issues, the clinical value of TTFM has been demonstrated in studies that found that TTFM predicted graft failure at 3, 6, and/or 12 months post-CABG.[118–120] Inadequate graft flow as defined by PI >5 on TTFM was found to be an independent predictor of major adverse cardiac events, operative death in particular.[121] No studies have yet explored the impact of IFI measurements on clinical outcomes during the follow-up. In general, randomized comparisons between CABG with and without graft flow measurement remain absent. Such studies would be required to evaluate the true benefit their routine intra-operative use would have on early and late rates of reintervention, myocardial infarction and death. One issue that remains, however, is that long-term graft failure would still occur as caused by other mechanisms than those controlled by intra-operative graft assessment. This could be one of the reasons why surgeons doubt its clinical impact and consequently why routine use has been limited.

## Secondary prevention

Apart from technical and procedural considerations, further optimization of long-term outcomes after CABG can be achieved through a strict medical regimen. Progression of atherosclerosis in the native coronary arteries continues after CABG and is associated with deterioration of left ventricular function. However, this can be prevented by the administration of antiplatelet agents,[122] β-blockers,[123] angiotensin-converting enzyme inhibitors (ACE-I),[124] statins[125,126] and fatty acids,[127] all of which have been identified as independent predictors of survival after CABG. The PREVENT IV trial found that secondary prevention medications were associated with significantly reduced rates of death or myocardial infarction after CABG.[128] Moreover, data suggest that graft patency may be better in patients taking statins,[129] fatty acids,[130] aspirin,[65] and possibly dual antiplatelet therapy.[131] Administration of secondary prevention medications has increased remarkably,[132,133] and differences between PCI and CABG have shown to converge (*Table 4*). Nevertheless, some data have shown that differences between PCI and CABG still remain and again stressed the need for further progress (*Figure 2*).[134–136]

Furthermore, the effect of lifestyle interventions on outcomes may be underestimated. A plethora of data exists on the impact of lifestyle intervention on outcomes after CABG. Van Domburg *et al.*,[137] for example, reported that patients who quit smoking had significantly improved 30-year survival when compared with persistent smokers after CABG [HR = 0.60 (95% CI: 0.48–0.72)]. Education and counselling on eliminating risk factors, healthy food choices, stress relief and exercise provide substantial benefit for patients.[138] A meta-analysis that combined 63 randomized clinical trials with follow-up data on 21 295 patients found that implementation of secondary prevention programmes significantly reduced all-cause mortality [risk ratio (RR) = 0.85 (95% CI: 0.77–0.94)] and myocardial infarction [RR = 0.83 (95% CI: 0.74–0.94)].[139] Notably, specific patient subgroups may benefit most from rigorous behavioural modifications: young (age <60 years) or old (age ≥75 years) patients, patients with a sedentary lifestyle and/or a smoking habit, patients with a low Mediterranean diet score and those who live alone.[140] However, data from three EUROASPIRE surveys showed that there was a clear need for more effective lifestyle management among patients with previous coronary revascularization.[141] The authors rightfully stated that treatment of coronary artery disease 'without addressing the underlying causes of the disease is futile; we need to invest in prevention'.

Initiatives should be undertaken to increase the rate of prescribing appropriate discharge medications and to emphasize the need for long-term medication compliance and lifestyle changes. In particular, home-based programmes may be efficient and more acceptable to

**Table 4** **Trends in the use of secondary preventive medication and the difference between coronary artery bypass grafting and percutaneous coronary intervention**

| | EUROASPIRE I 1995–96, *n* = 9 countries | EUROASPIRE II 1999–2000, *n* = 15 countries | EUROASPIRE III 2006–07, *n* = 22 countries |
|---|---|---|---|
| Antiplatelets (%) | | | |
| CABG | 87.9 | 86.8 | 92.9 |
| PCI | 89.4 | 90.0 | 94.9 |
| Δ | −1.5 | −3.2 | −2.0 |
| Beta-blockers (%) | | | |
| CABG | 56.5 | 68.0 | 90.7 |
| PCI | 61.7 | 73.6 | 84.4 |
| Δ | −5.2 | −5.6 | +6.3 |
| Blood pressure-lowering drugs (%) | | | |
| CABG | 86.2 | 90.1 | 98.7 |
| PCI | 87.4 | 91.3 | 95.9 |
| Δ | −1.2 | −1.2 | +2.8 |
| Lipid-lowering drugs (%) | | | |
| CABG | 36.7 | 67.6 | 90.5 |
| PCI | 42.2 | 69.9 | 89.4 |
| Δ | −5.5 | −2.3 | +1.1 |

Data from Kotseva *et al.*[133]
CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

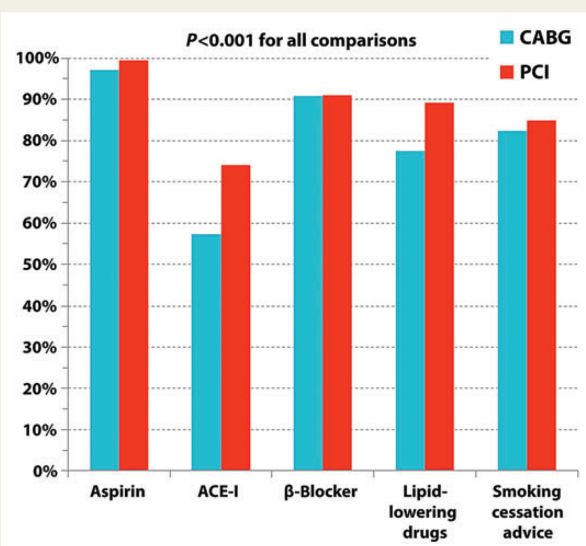


**Figure 2** Difference in secondary prevention measures after percutaneous coronary intervention and coronary artery bypass grafting. Data from Hiratzka *et al.*[134] ACE-I, angiotensin-converting enzyme inhibitor; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

patients—with the additional benefit of lower costs.[142] Such quality improvement programmes can be easily instated and could potentially improve patient care significantly.

# Decision-making

Despite the potential for further optimization of CABG outcomes, PCI will remain an excellent alternative in specific patients. Evidence suggests that there is overuse, underuse and inappropriate selection of revascularization strategies.[143] Inappropriate use and underuse may partly explain the preferences expressed by patients,[144] who prefer less invasive techniques with minimized pain over the long-term prospect of improved survival. In that respect, MIDCAB or hybrid procedures may present an alternative, but often patients are not even informed about the survival advantage with CABG.[145] Naturally, if two treatments are considered to produce similar results, patients will opt for the least invasive.

Reflecting on the current revascularization guidelines, recent trial results and weighting risk–benefit ratios of (new) developments, *Figure 3* provides a proposal for a decision-tree for revascularization. The myriad of treatment options emphasize the need for targeted patient selection, and the mix of surgical and interventional therapies provides rationale for multidisciplinary Heart Team decision-making to discuss all potential treatment options and obtain informed consent. Clinical cardiologists, interventional cardiologists and cardiovascular surgeons should convene on a regular basis to recommend the most appropriate treatment strategy for individual patients.[143,146] The importance of a Heart Team was once more stressed in the SYNTAX trial[147] and was subsequently included in the European and American guidelines.[3,148] Practice may be different across centres and countries, and a local protocol should be established to define patient populations that are candidates for certain

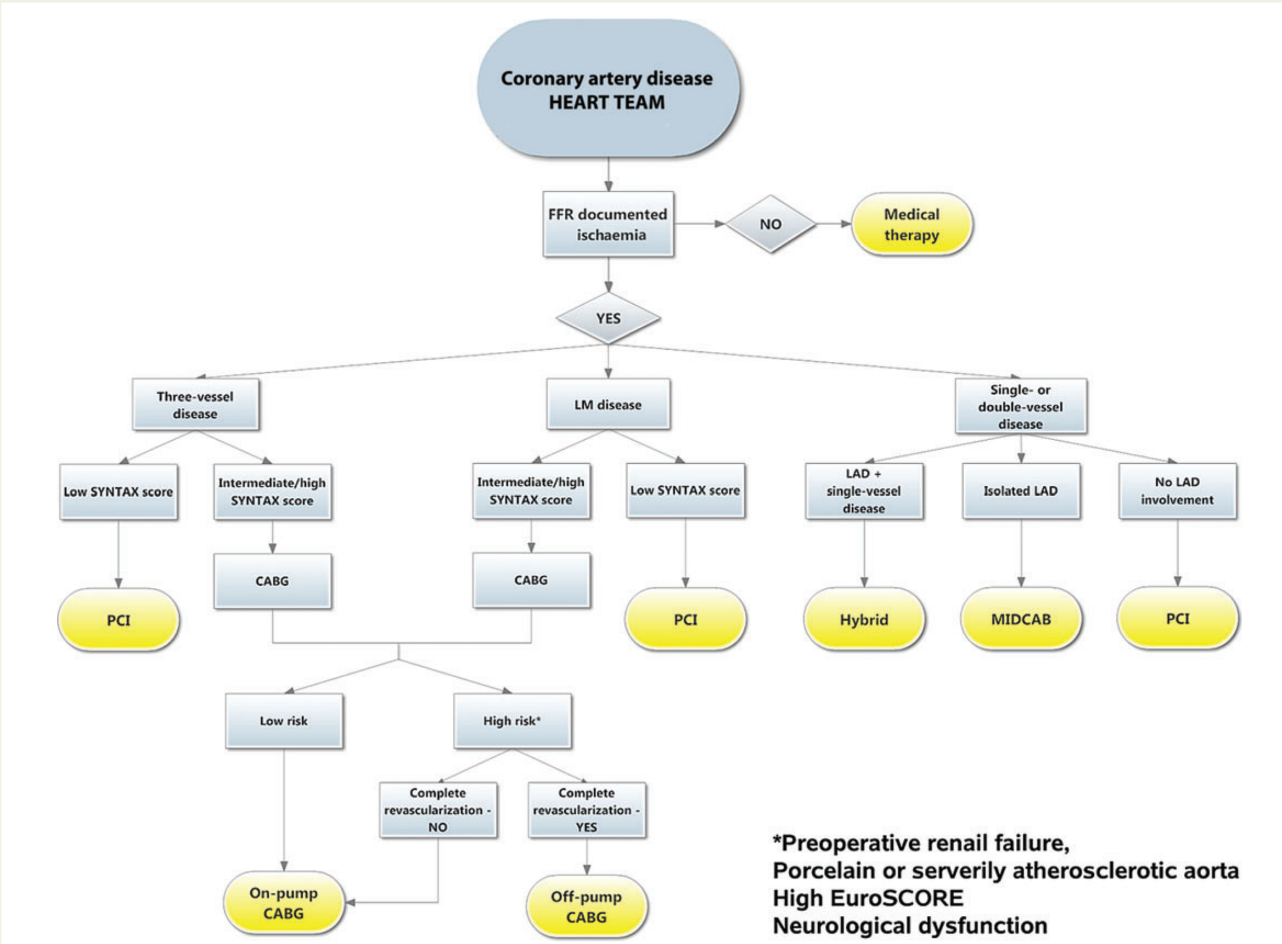


**Figure 3** Proposal for a decision-tree for revascularization. Some of these recommendations have not yet been validated and still require randomized evaluation. CABG, coronary artery bypass grafting; LAD, left anterior descending; LM, left main; MIDCAB, minimally invasive coronary artery bypass; PCI, percutaneous coronary intervention.

therapies. The various pros and cons of surgical revascularization strategies should then be considered by the Heart Team (*Table 5*).

# Future studies

Rigorous evaluation of potential advancements remains crucial before they are introduced on a wide scale. Even an extensive body of evidence supporting some interventions is not necessarily sufficient to provide evidence-based recommendations. This is exemplified by the >60 randomized trials comparing off-pump with on-pump surgery:[13,30,35] a benefit of off-pump CABG has been suggested in many studies that included different patient populations. Nevertheless, the two latest and largest randomized trials that included low- and high-risk patients found no difference between the two treatment options.[30,35]

In contrast, data on some new therapeutic strategies remain scarce, but the existing data may demonstrate excellent safety and efficacy. Such results often represent outcomes from highly selected patients treated by experienced surgeons in high-volume centres. This introduces a bias; the generalizability of such results is limited and caution is advised. An example of this is the evaluation of TECAB procedures.

## Percutaneous coronary intervention vs. coronary artery bypass grafting studies

Continuous evaluation of PCI vs. CABG calls for a specific focus on new developments in both interventions. For PCI patients, new stents will become available and the use of fractional flow reserve to assess the need and completeness of revascularization is emphasized.[149,150] Equivalent data on FFR-guided CABG are scarce.[151] Future studies should explore the use and differences of FFR-guided revascularization between PCI and CABG.[152] The impact of the degree of ischaemia and viability on the outcomes of both CABG and PCI in patients with stable angina is still under debate. Whether image-guided revascularization that is based on a combination of functional and anatomical imaging—for example, position emission tomography computed tomography (*Figure 4*)—can improve the outcomes as compared with the traditional occlustenotic approach warrants further trials.

**Table 5** Pros and cons of different surgical revascularization techniques

| | Conventional CABG | Off-pump CABG | MIDCAB | TECAB | Hybrid revascularization |
|---|---|---|---|---|---|
| Lesions | Multivessel disease (+) | Multivessel disease (+) | Isolated LAD stenosis (+/−) | Multivessel disease (+) | Multivessel disease (+) |
| Technical difficulty | None (+) | Moderate (+/−) | Moderate (+/−) | Difficult (−) | Moderate (+/−) |
| Incision | Sternotomy (−) | Sternotomy (−) | J-incision (+/−) | Endoscopic (+) | J-incision (+/−) |
| Cardiopulmonary bypass | Yes (−) | No (+) | No (+) | No (+) | No (+) |
| Procedure time | Short (+) | Prolonged (+/−) | Long (−) | Long (−) | Long (−) |
| Blood products | Many (−) | Less (+/−) | Few (+) | Few (+) | Few (+) |
| Completeness of revascularization | Complete (+) | Complete (+) or incomplete (+/−) | Complete (+) or incomplete (+/−) | Complete (+) or incomplete (+/−) | Complete (+) |
| Postoperative length of stay | Long (−) | Prolonged (+/−) | Short (+) | Short (+) | Short (+) |
| Postoperative pain | Yes (−) | Yes (−) | Yes (−) | Less (+/−) | Yes (−) |
| Recovery time | Long (−) | Long (−) | Short (+) | Short (+) | Short (+) |
| Rate of stroke | High (−) | Less (+/−) | Less (+/−) | Less (+/−) | Less (+/−) |
| Rate of repeat revascularization | Good (+) | Moderate (+/−) | Good (+) | Moderate (+/−) | Moderate (+/−) |

The various features are scored as following: in favour of the technique (+), reasonable in favour (+/−), detrimental for the technique (−).
CABG, coronary artery bypass grafting; LAD, left anterior descending; MIDCAB, minimally invasive coronary artery bypass.

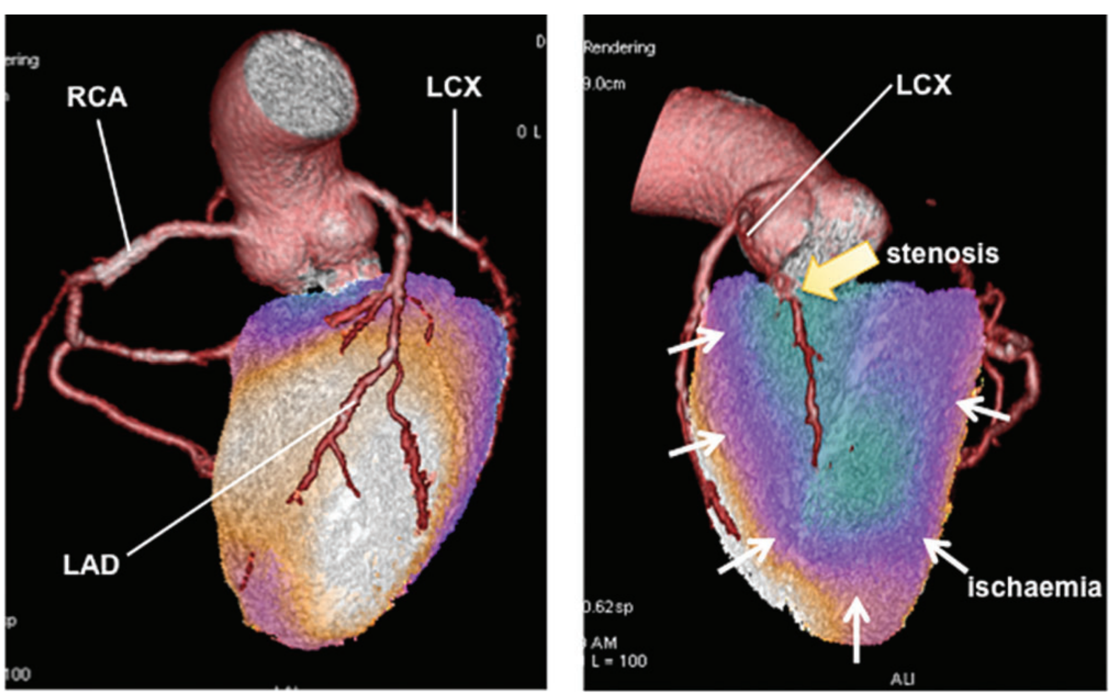


**Figure 4** Functional and anatomical imaging using position emission tomography computed tomography. Case: 70-year-old male had atypical symptoms of three-vessel coronary artery disease for which he underwent stenting of the right coronary artery in 2012. Scan is positive for inferolateral wall ischaemia (purple). LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Traditionally, trials are limited to their internal validity, i.e. the results are only applicable to the included patient cohort; large 'real-world' registries are required to demonstrate whether trial results are also applicable to the general population.[10] Alternatively, an 'all-comers' trial design with none to limited patient exclusion criteria increases external validation, and presents a more balanced trade-off

**Table 6** **American and European guideline recommendations**

| | Guidelines | |
|---|---|---|
| | **American** | **European** |
| Off-pump CABG | 'In patients with preoperative renal dysfunction (creatinine clearance $<$60 mL/min), off-pump CABG may be reasonable to reduce the risk of acute kidney injury' **IIb B**<br>'It is reasonable to consider off-pump CABG to reduce perioperative bleeding and allogeneic blood transfusion' **IIa A** | 'Off-pump CABG may be considered, rather than on-pump CABG for patients with mild-to-moderate chronic kidney disease' **IIb B** |
| MIDCAB | No recommendation | No recommendation |
| Hybrid revascularization | 'Hybrid coronary revascularisation is reasonable in patients with 1 or more of the following: limitations to traditional CABG, such as heavily calcified proximal aorta or poor target vessels for CABG (but amenable to PCI); lack of suitable graft conduits; unfavourable LAD artery for PCI (i.e. excessive vessel tortuosity or chronic total occlusion)' **IIa B**<br>'Hybrid coronary revascularization may be reasonable as an alternative to multivessel PCI or CABG in an attempt to improve the overall risk–benefit ratio of the procedures' **IIb C** | 'Hybrid procedure, defined as consecutive or combined surgical and interventional revascularization may be considered in specific patient subsets at experienced centres' **IIb B** |
| Clampless/'no touch' | 'Patients with extensive disease of the ascending aorta pose a special challenge for on-pump CABG; for these patients, cannulation or cross-clamping of the aorta may create an unacceptably high risk of stroke. In such individuals, off-pump CABG in conjunction with avoidance of manipulation of the ascending aorta (including placement of proximal anastomoses) may be beneficial' (**no formal recommendation, no level of evidence**) | No recommendation |
| Endoscopic vein harvesting | No recommendation | 'Endoscopic vein-graft harvesting cannot be recommended at present as it has been associated with vein-graft failure and adverse clinical outcomes' (**no formal recommendation, no level of evidence**) |
| Epiaortic scanning | 'Routine epiaortic ultrasound scanning is reasonable to evaluate the presence, location, and severity of plaque in the ascending aorta to reduce the incidence of atheroembolic complications' **IIa B** | No recommendation |
| Graft flow assessment | No recommendation | 'Graft evaluation is recommended before leaving the operating theatre' **I C** |
| Arterial revascularization | 'If possible, the LIMA should be used to bypass the LAD artery when bypass of the LAD artery is indicated' **I B**<br>'When anatomically and clinically suitable, use of a second IMA to graft the left circumflex or right coronary artery (when critically stenosed and perusing LV myocardium) is reasonable to improve the likelihood of survival and to decrease reintervention' **IIa B**<br>'Complete arterial revascularization may be reasonable in patients $\leq$60 years of age with few or no comorbidities' **IIb C** | 'Arterial grafting to the LAD system is indicated' **I A**<br>'Complete revascularization with arterial grafting to non-LAD coronary systems is indicated in patients with reasonable life expectancy' **I A** |

| | | |
|---|---|---|
| Secondary prevention | 'All smokers should receive in-hospital educational counselling and be offered smoking cessation therapy during CABG hospitalization' **I A**<br>'[Aspirin] should be initiated within 6 h postoperatively and then continued indefinitely to reduce the occurrence of SVG closure and adverse cardiovascular events' **I A**<br>'All patients undergoing CABG should receive statin therapy, unless contraindicated' **I A**<br>'β-blockers should be prescribed to all CABG patients without contraindications at the time of hospital discharge' **I C**<br>'ACE inhibitors and ARBs should be initiated postoperatively and continued indefinitely in CABG patients who were not receiving them preoperatively, who are stable, and who have an LVEF ≤40%, hypertension, diabetes mellitus, or CKD, unless contraindicated' **I A** | In general, an 'ABCDE' approach is proposed: 'A' for antiplatelet therapy, anticoagulation, ACE inhibition, or angiotensin receptor blockade; 'B' for beta-blockade and blood pressure control; 'C' for cholesterol treatment and cigarette smoking cessation; 'D' for diabetes management and diet; and 'E' for exercise.<br>Several recommendations are provided with regard to lifestyle and risk factor management (e.g. counselling on physical activity and exercise training, **I A**; diet and weight control management, **I B**; smoking cessation, **I B**).<br>'Secondary prevention demands lifelong antiplatelet therapy with 75-325 mg acetylsalicylic acid daily'<br>'ACE inhibitors should be started and continued indefinitely in all patients with LVEF ≤40% and for those with hypertension, diabetes, or CKD, unless contraindicated' **I A**<br>'It is indicated to start and continue β-blocker therapy in all patients after MI or ACS or left ventricular dysfunction, unless contraindicated' **I A**<br>'High-dose lipid lowering drugs are indicated in all patients regardless of lipid levels, unless contraindicated' **I A**<br>'Fibrates and omega-3 fatty acids (1 g/day) should be considered in combination with statins and in patients intolerant of statins' **IIb B** |

The level of evidence is shown in bold. ACE, angiotensin-converting enzyme; ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; LAD, left anterior descending; LVEF, left ventricular ejection fraction; (L) IMA, (left) internal mammary artery; MI, myocardial infarction; PCI, percutaneous coronary intervention.

between internal and external validation.[153] Furthermore, reporting the experience of centres and operators will also contribute to the internal and external validity of trial results: superior outcomes in experienced centres as opposed to inexperienced centres unveils limited external validity and should restrict one from over-extrapolating trial results to real-world clinical settings.

In the SYNTAX trial a new angiographic score was validated—the SYNTAX score—for grading the complexity of coronary artery disease.[154] This score appears to be a very promising tool for deciding if PCI or CABG would be preferable. Use of the score is therefore recommended for decision-making. Recently, the SYNTAX II score was introduced and showed an improvement in guiding decision-making.[155] Yet, further validation of these hypothesis-generating data is needed and future studies should provide a larger body of evidence about the SYNTAX (II) score.

Pharmacological management of patients after PCI and CABG differs significantly and has an impact on long-term results. It would be interesting to see the results of PCI and CABG if the pharmacological management and treatment adherence after PCI and CABG would be identical.

# Discussion

Broadening indications for and increasing use of PCI calls for more focus on the optimization of short- and long-term outcomes after CABG. Expanding the use of lesser invasive techniques may persuade patients to accept surgery as the preferable treatment option. Particularly studies comparing PCI with CABG require the most optimal surgical revascularization strategy to show superiority over PCI. Arterial revascularization with minimized aortic manipulation and intra-operative graft flow measurement is a relatively easy way to improve outcomes.

Adoption rates of new techniques have been low, despite all advances. This may be due to: (i) the familiarity that surgeons have with existing techniques, a reluctance to change and the willingness to go through the learning curve typical for a new technique, (ii) the more demanding nature of some technical advances, (iii) complications related to the use of a new technique and/or device, (iv) time-consuming steps that may have to be carried out during the procedure, and (v) logistic reasons with regard to the need for additional equipment, planning and sterility. Particularly when the presumed benefits with new techniques are not yet clearly proven, these factors play a major role in maintaining existing protocols. However, the benefit of advancements will often become evident when overcoming the learning curve. On the other hand, some techniques will always be time-consuming and reserved for highly specialized centres.

## Guidelines

One explanation for the underuse of new techniques and secondary prevention measures may be the lack of data supporting their benefit. This calls for large registries and randomized trials to provide additional rigorous evaluation of, in particular, MIDCAB, hybrid revascularization, epiaortic scanning and graft flow measurement. Another reason for lack of widespread implementation and geographic variations may be the differing recommendations of the American and European guidelines concerning their use (*Table 6*). This is illustrated

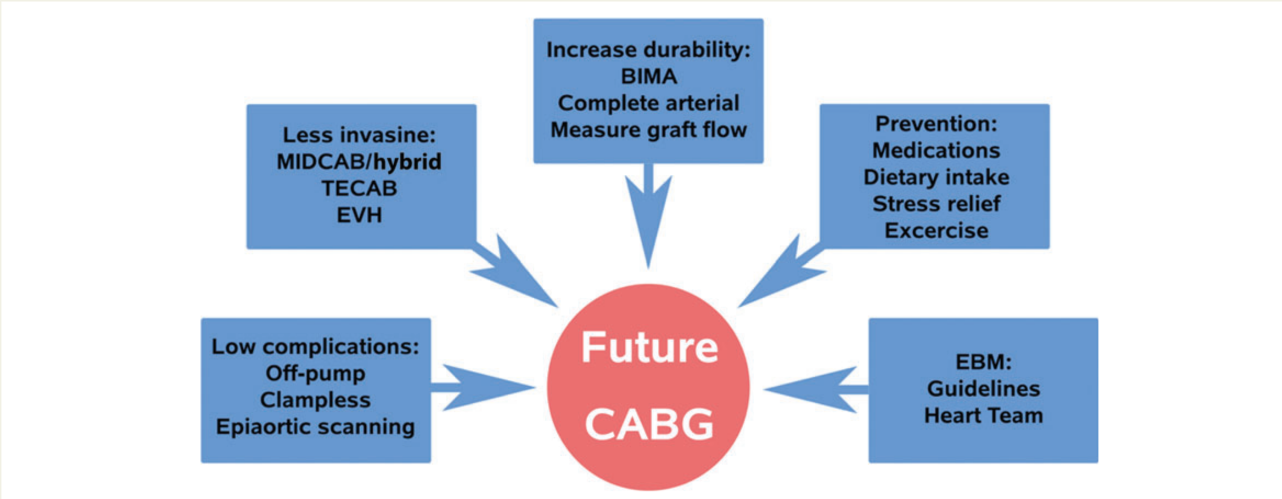


**Figure 5** Summary of developments to optimize short- and long-term results after coronary artery bypass grafting. BIMA, bilateral internal mammary artery; CABG, coronary artery bypass grafting; EBM, evidence-based medicine; EVH, endoscopic vein harvesting; MIDCAB, minimally invasive coronary artery bypass; TECAB, totally endoscopic coronary artery bypass.

by recommendations for epiaortic scanning and graft flow assessment. The current European ESC/EACTS revascularization guidelines include a class 1C recommendation for intra-operative graft flow assessment [3] and the American guidelines state that 'epiaortic ultrasound is reasonable to evaluate. . .', which translates to a class IIa B recommendation.[148] However, the American guidelines do not include a recommendation for graft flow assessment, while the European guidelines lack a recommendation for epiaortic scanning.

## Patient, cost, and market considerations

Adoption of minimally invasive techniques that result in lower post-operative complications and reduced length of stay will significantly improve patient satisfaction, and raise patients' willingness to undergo CABG as opposed to PCI. On the background of the issue of rising healthcare expenditures, these improvements may also help reduce overall costs.

Continued optimization of short- and long-term outcomes of CABG will reduce costs for health insurance providers who may therefore favour adoption of new techniques associated with shorter initial in-hospital stays, reduced complication rates and fewer repeat revascularizations. In addition, pay for performance is increasingly instated.[156] This system provides additional incentives to innovate and improve outcomes.

Containing costs to both health insurance providers and societies may in some healthcare systems require a reduction of the number of centres performing CABG. Innovation and integrating technological advances into everyday clinical practice may be rewarded by certification as a centre of excellence, by continued issuance of a practice licence and by more patient referrals. Implementation of the Heart Team decision-making process may furthermore strengthen the position of a centre. This approach highlights the centre's collaborative environment between specialties, which is appreciated by patients.[143] There may also be major cost implications by eradicating suboptimal treatment: healthcare costs will be contained as rates of adverse events requiring rehospitalization and additional procedures are reduced.

## Conclusion

Outcomes after surgical revascularization have the potential to improve beyond the level achieved during recent decades (*Figure 5*). However, to facilitate these improvements, surgeons need to be willing to adopt new techniques that increase procedural safety, patient satisfaction, and long-term survival. To achieve these goals, guidelines should be conclusive about recommending certain techniques and provide guidance for their use. Future trials will need to provide sufficient evidence for such recommendations by focussing on specific areas where optimal therapy has yet to be substantiated.

**Conflict of interest:** none declared.

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